Table S1: Locus sequencing at potential off-target sites for the insulator sgRNA, related to Figure 2
Locus sequencing data shows lack of edits at potential off-target sites with a PAM for the insulator sgRNA.
N.D = not detected.

	Number of Mismatches (MM)	Binding sites in genome with adjacent PAM site	Chromosome coordinates of target sites with PAM (mm10)	Features of target site	CTCF peak in targeted region	Mutation frequency in Cas9-NT (%)	Mutation frequency in Cas9-Insulator (%)
On target	0	1	chr5:75210053	targeted PDGFRA insulator site	Yes	N.D	100%
Off target	1	0	-	-	-	-	-
	2	0	-	-	-	-	-
	3	0	-	-	-	-	-
	4	5	chr2:123471441	Intergenic	No	N.D	N.D
			chr12:32686058	Intergenic	No	N.D	N.D
			chr17:85028268	promoter of *Slc3a1*	No	N.D	N.D
			chr6:10747137	Intergenic	No	N.D	N.D
			chr10:23307984	Intron of *Eya4*	No	N.D	N.D

Table S2: Locus sequencing at potential off-target sites for the RFXmotif sgRNA, related to Figure 2

Locus sequencing data shows lack of edits at potential off-target sites for the RFXmotif sgRNA, with exception of an intronic site with low-level editing. N.D = not detected. (*) = evaluated using ChIP-seq sequencing data.

	Number of Mismatches (MM)	Binding sites in genome with adjacent PAM site	Chromosome coordinates of target sites with PAM (mm10)	Features of target site	H3K27ac peak in targeted region	Mutation frequency in Cas9-NT (%)	Mutation frequency in Cas9-RFXmotif (%)
On target	0	1	chr5:75223009	targeted enhancer	Yes	0%	100%
Off target	1	0	-	-	-	-	-
	2	1	chr9:57715379	Intron of *Edc3*	No	N.D	<10%
	3	12	chr8:123069125	Intron of *Spg7* *	No	N.D	N.D
			chr5:71780635	Intron of *Gabrb1*	No	N.D	N.D
			chr1:23835089	Intron of *B3gat2*	No	N.D	N.D
			chr1:51596428	Intergenic	No	N.D	N.D
			chr2:127890371	Intron of Acoxl	No	N.D	N.D
			chr2:167747246	Intergenic*	Yes	N.D	N.D
			chr12:85571470	Intergenic*	Yes	N.D	N.D
			chr4:142838737	Intergenic	No	N.D	N.D
			chr6:119023380	Intron of Cacna1c	No	N.D	N.D
			chr11:74400961	Intron of *Rap1gap2*	No	N.D	N.D
			chr19:10299031	Intron of Dagla	No	N.D	N.D
			chr3:138803897	Intron of *Tspan5* *	Yes	N.D	N.D

Table S3: Off-target analysis for the 3A3L-pCdkn2a sgRNAs, related to Figure 3
sgRNA off-target analysis shows that the sgRNAs used for epigenetic editing do not have off-target sites with complementarity to both sgRNAs allowing up to 6 mismatches per gRNA.

		Number of Mismatches (MM)	Binding sites in genome with adjacent PAM site (within 1 KB of both guides)	Chromosome coordinates of target sites with PAM (mm10)	Features of target site	H3K27ac peak in targeted region
Convergent guides	**On target**	0	1	Chr4:89294696-89294848	targeted promoter	Yes
	Off target	1	0	-	-	-
		2	0	-	-	-
		3	0	-	-	-
		4	0	-	-	-
		5	0	-	-	-
		6	0	-	-	-